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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,480	03/12/2001	Michael P. Maher	AUROBIO.026DV1	1223

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EXAMINER

MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,480	MAHER ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 9-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>041904 032502 0813</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-8, in the response submitted 04/22/2004 is acknowledged.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Sinha et al. (1995).

Sinha et al. developed a system for simultaneous optical recording of transients of membrane potential and intracellular calcium concentration from mammalian brain slice preparations with high spatio-temporal resolution. In the method of Sinha et al. simultaneous recording was achieved by using two dedicated photodetectors together with two fluorescent indicators. Specifically, the calcium-sensitive dye Calcium Orange and the voltage-sensitive dye RH-414 were used because they have overlapping excitation spectra, but separable emission spectra. The method of Sinha et al. anticipates claim 1 because the method uses cells (specifically, hippocampal slices, see page 53), the cells are exposed to a compound (the glutamate antagonists CNQX and d-APV, see page 56, Figure 5), and the cells are exposed to an electric field in this instance an a single stimulus is delivered via an electrode to the stratum

radiatum area. The method of Sinha also measures transmembrane potential because the cells are loaded with dyes sensitive to transmembrane potential, and the fluorescence is measured (see page 56, Figure 5). Claims 2-5 are anticipated because the cells comprise a voltage gated ion channel which will be released from inactivation in response to the stimulation, and the measuring was done using a transmembrane potential dye. Claims 6-8 are anticipated because the responses are stimulated with 500 micro sec current pulses delivered at frequencies less than 0.05 Hz (page 53, column 2, last paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/41166 (Tsien et al.).

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Tsien et al. teaches methods of assaying for small changes in transmembrane potential using voltage sensitive dyes (page 3, lines 1-25), and measurement of T_m using FRET (page 37, lines 25-36). Tsien et al. teach methods of screening for potential therapeutic drugs that affect membrane potentials in living cells (page 42). Tsien et al. further teach the use of cells which have been transfected with nucleic acids encoding, *inter alia*, ion channels (page 44, lines 1-5). Tsien et al. further teaches the use of cell lines including HEK293, LM(TK-), COS, and CHO cells (page 44, lines 7-11). Tsien et al. teaches that the transfected cells are treated with a stimulus that modulates the ion channel (page 43, lines 15-20). Tsien et al. teaches that the ion channel may be a sodium, potassium, or calcium channel, which may be voltage-gated (page 43, lines 27-31). While Tsien et al. does not set forth the stimulation protocols it is a designer's choice to use an electric field to stimulate the ion channel, given that it is known in the art to use electric fields to stimulate voltage gated ion channels, as evidenced by Jacobs et al. Jacobs et al. teaches the electric field stimulation of cultured cells to stimulate Ca^{++} transients (see page 4130, column 1, second paragraph and page 4131, Figure 1). Thus it would have been obvious to one of skill in the art at the time the invention was made to practice a method of assaying a compound agent for activity against an ion channel wherein the cells are activated with an electric field, and the transmembrane potential is measured using FRET. The motivation is provided in the Tsien et al. reference that teaches that the method is sensitive to small changes in transmembrane potentials, and can respond on a rapid, millisecond timescale to changes in membrane potentials (page 2, lines 30-38).

Conclusion

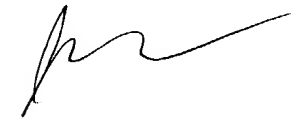
No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
June 25, 2004